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Relationship Between External and Internal Parameters of Exposure to Manganese in Workers From a Manganese Oxide and Salt Producing Plant

Harry Roels, PhD, Robert Lauwerys, MD, DS, Pierre Genet, MD, Mohammad Jawad Sarhan, MD, Michèle de Fays, MD, Isabelle Hanotiau, MD, and Jean-Pierre Buchet, PhD

In a plant producing manganese (Mn) oxides and salts, 11 different workplaces were identified. The current exposure to airborne Mn (total dust, personal sampling, n = 80) varied from 0.07 to 8.61 mg/m^3. The geometric mean and median values amounted approximately to 1 mg/m^3 and the 95th percentile was 3.30 mg/m^3. The concentration of Mn in blood (Mn-B) in a group of 141 Mn-exposed male workers ranged from 0.10–3.59 μg/100 ml compared to 0.04–1.31 μg/100 ml in a group of 104 control subjects. The ranges of the concentrations of Mn in urine (Mn-U) were 0.06–140.6 and 0.01–5.04 μg/g creatinine for the exposed and control groups, respectively. The average level of Mn-B in the Mn group was more than twice as high as in the control group (arithmetic mean, 1.36 vs 0.57 μg/100 ml) and that of Mn-U was ten times higher in the Mn group (geometric mean, 1.56 vs 0.15 μg/g creatinine). The Mn-B level did not change significantly after 8 h of Mn exposure, whereas the Mn-U level dropped rapidly when exposure ceased (half-life less than 30 h).

On an individual basis, neither Mn-B nor Mn-U correlated with the current levels of Mn-air or duration of Mn exposure. There was also no relationship between Mn-B and Mn-U. On a group basis, there was no correlation between the mean Mn-B levels and the current levels of Mn-air at each workplace; however, a slight but significant correlation ($r = 0.62$, $p < 0.05$) was found between the geometric mean of Mn-U of each subgroup (n = 11) and the current level of Mn-air at their corresponding workplaces. On a group basis (n = 6), Mn-U did not correlate with the estimation of past integrated exposure of the workers, while group means of Mn-B significantly correlated with past integrated exposure. These results indicate that the individual evaluation of the Mn exposure intensity remains difficult on the basis of Mn-B and Mn-U. On a group basis however, Mn-U appears to reflect very recent exposure, while Mn-B is to some extent a reflection of the body burden of Mn.

Key words: occupational Mn exposure, Mn in blood, Mn in urine

Unité de Toxicologie Industrielle et Médecine du Travail, Faculty of Medicine, University of Louvain, Brussels, Belgium.
The current address for Dr. M.J. Sarhan is the Department of Public Health and Community Medicine, College of Medicine Almustansiriya University, P.O. Box 14132, Baghdad, Iraq.
Address reprint requests to Harry Roels, Unité de Toxicologie Industrielle et Médecine du Travail, Faculty of Medicine, University of Lourain, Clos Chapelle-aux-Champs 30.54, 13 - 1200 Brussels, Belgium.
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INTRODUCTION

Workers absorb manganese (Mn) mainly through the lungs, although additional absorption via the gastrointestinal tract may occur to some extent (mucociliary clearance of the lungs, direct ingestion of dust particles). The absorption of Mn via the lungs and the gut is poorly understood [WHO, 1981; US-EPA, 1984]. The rate of gastrointestinal absorption is lower than 5%, but it may be higher in iron-deficient persons [Mena et al, 1969; Thomson et al, 1971]. Once entered into the blood circulation, Mn is cleared from the blood within a few min [Cotzias et al, 1968; Gibbons et al, 1976] and concentrates rapidly in the liver where the primary homeostatic mechanism is exerted at the level of excretion via the bile [Britton and Cotzias, 1966; Papavasiliou et al, 1966; Leach, 1976]. Another regulatory site may be at the level of gastrointestinal absorption [Abrams et al, 1976]. Part of the Mn excreted with the bile probably undergoes enterohepatic circulation [Cikrt, 1973]. Whatever the route of absorption, the elimination of Mn is almost exclusively via the feces. Animal [Klaassen, 1974] and human studies [Tipton et al, 1969; McLeod and Robinson, 1972] have demonstrated that the kidneys are not an important route for the elimination of Mn. According to Buchet et al [1976], Tsalev et al [1977], and Watanabe et al [1978], the normal concentrations of Mn in whole blood and in urine are less than 2 μg/100 ml and 3 μg/l, respectively.

Although the excretion in urine is low, some authors have considered urinary manganese (Mn-U) to reflect recent exposure [Tanaka and Lieben, 1969; Horiuchi et al, 1970; Smyth et al, 1973]. Horiuchi et al [1970] found statistically significant correlations between the neurological findings and the levels of Mn in blood and in urine. The studies of Jonderko et al [1971] and Smyth et al [1973] did not confirm that relationship between manganese concentration in blood (Mn-B) and neurological symptoms. Smyth et al [1973] found in Mn-exposed workers no significant correlation between Mn-B and the level of Mn-air; the mean Mn-B level (4 μg/100 ml) did not differ appreciably from that of a control group (3 μg/100 ml). In workers exposed over the last 5 years to an average concentration of 1 mg Mn/m^3 in a Mn alloy plant, Tsalev et al [1977] found mean Mn-B values of 1.1–1.6 μg/100 ml (1 μg/100 ml in nonexposed subjects). There was no evidence of an increase of Mn-B with length of employment. In workers from a similar plant, Jonderko et al [1971] reported that Mn-B increased only after more than 4 years of exposure and quickly dropped when exposure ceased. Ulrich et al [1979] reported that blood Mn levels in monkeys and rats exposed by inhalation to Mn_3O_4 aerosol increased in a dose-related manner.

The only conclusion that can be drawn from the above data is that the biological significance of Mn-U and Mn-B is far from clear.

The present study attempts to examine the relationship between environmental (Mn-air, duration of exposure) and biological (Mn-B, Mn-U) parameters in workers from a plant producing Mn oxides and salts.

MATERIALS AND METHODS

Description of the Factory and Production Processes

The factory is one of the major world producers of manganese oxides and salts with a total workforce of about 150 male employees. Crude concentrated manganese

dioxide ores are used from which, through different chemical treatments, manganese sulfate, nitrate, carbonate, and oxides (Mn_3O_4, MnO_2) are prepared. During the production process, the workers are exposed to airborne manganese dust when ores and intermediate products are mechanically transferred and when the final products are bagged. Some production steps involve thermal or wet procedures. It should be pointed out that this plant started production in 1964 and that the initial production process and the various buildings are still in use, although significant additions have been made to them.

Study Population

A group of 141 Mn-exposed male subjects was examined including production staff and research and development personnel (engineers, laboratory technicians, foreman-operators), workers mainly engaged in transport and handling (laborers), and workers mainly occupied with repair and maintenance. Job turnover within the plant is considerable; about 40% of the employees have worked at more than one work site in the plant. A control group of 104 male workers was recruited from a nearby chemical plant. The mean (range) age was 38.4 years (19–58) and 34.3 years (19–59) for the control and Mn-exposed groups, respectively. The average duration of exposure to manganese was 7.1 years (range 1–19). Both groups were matched for socioeconomic status and background environmental factors.

Collection of Samples and Analytical Methods

Eleven different workplaces could be identified in the manganese plant from which a total of 80 personal air samples were taken. The total airborne manganese concentration was determined in the breathing zone of the workers with the use of personal air samplers Model C, T-13051 (Casella, London) equipped with a filter holder, Model T 13070 (Casella). Air was sampled at a flow rate of 1.2 to 2.4 l per min for 6.6 h on average (median 7.5 h, range 3–8 h; the air sampling lasted for more than 5 h for about 80% of the samples). Glass fiber filters (Whatman GF/A, 3.7 cm) were used for collection of particles. The filters were treated with 5 ml HNO_3 (65%, w/v) at 110°C and the dry residues dissolved in 15 ml HNO_3 0.05 N by warming and addition of a few drops of H_2O_2 (30%, w/v). The solutions were diluted 20 to 50 fold and their manganese content was determined by flame atomic absorption spectrometry (Varian Techtron, Model 1100) by reference to an external standard calibration line (0 to 5 μg Mn/ml).

Blood and spot-urine samples were taken in the medical department of the plant after each worker had taken a shower. They were analyzed for manganese by flameless atomic absorption spectrometry using the method of internal standard [Buchet et al, 1976]. Urinary creatinine was measured using the picrate method of Jaffe [Henry, 1965].

RESULTS

External Manganese Exposure

Figure 1 shows the cumulative frequency distribution of Mn-air (total dust, time-weighted average concentration). The airborne manganese levels ranged from 0.07 to 8.61 mg/m^3 with overall mean ± SD and median values of 1.33 ± 0.14 and 0.97 mg/m^3, respectively. The geometric mean value amounted to 0.94 mg/m^3 and

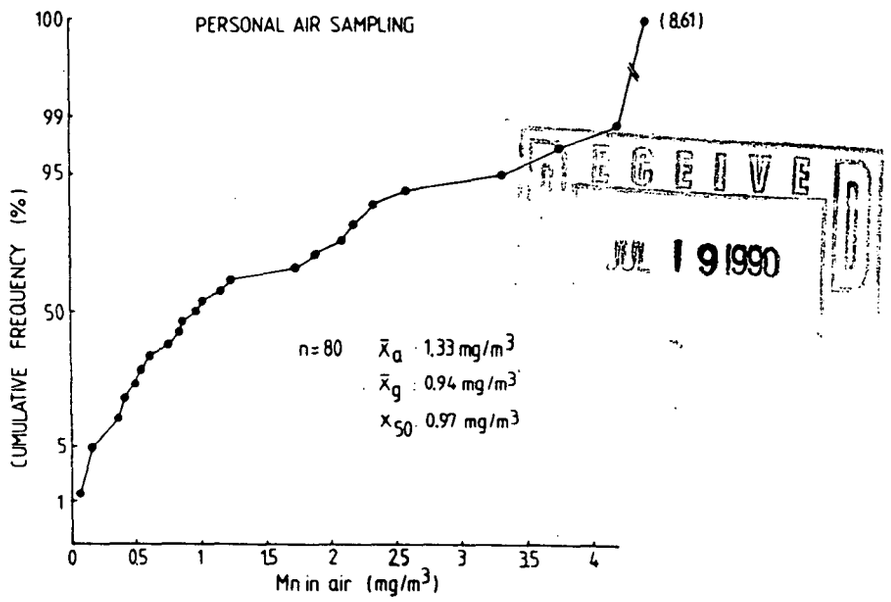

Fig. 1. Cumulative frequency distribution of time-weighted average concentration of manganese in air (total dust) measured at different workplaces of a manganese salt and oxide producing plant by means of personal air samplers. $\bar{X}_a$, arithmetic mean; $\bar{X}_g$, geometric mean; X_{50}, median.

the 95th percentile was 3.30 mg/m^3. In the control group, a total number of 22 whole-shift air samples were taken at representative workplaces showing that Mn-air levels ranged from 2 to 52 μg/m^3 with mean and median values of 12 and 7 μg/m^3, respectively (95th percentile:29 μg/m^3).

Internal Manganese Exposure

The internal exposure to manganese was estimated by the determination of manganese in blood and in urine. Figure 2 compares the cumulative frequency distributions of Mn-B and Mn-U for control and Mn-exposed workers, and shows a significant shift to higher values in the Mn group (χ^2 test, $P < 0.001$). The Mn-B levels ranged from 0.04 to 1.31 μg/100 ml in the control group and from 0.10 to 3.59 μg/100 ml in the Mn-exposed group. The arithmetic (SD) and geometric mean values for Mn-B were 0.57 (0.27) vs 1.36 (0.64) μg/100 ml and 0.49 vs 1.22 μg/100 ml, in the control and Mn-exposed groups, respectively. In the controls, the 95th percentile of Mn-B is 1.02 μg/100 ml. About 50% of the Mn-exposed workers had Mn-B levels above the highest value found in the control group. The Mn-U levels ranged from 0.01 to 5.04 μg/g creatinine in the control group and from 0.06 to 140.6 μg/g creatinine in the Mn-exposed group. The arithmetic mean values for Mn-U amounted to 0.30 vs 4.76 μg/g creatinine whereas the geometric mean (SDg) values were 0.15 (3.09) vs 1.59 (3.73) μg/g creatinine, in the control and Mn-exposed groups, respectively. In the controls, the 95th percentile of Mn-U is 0.85 μg/g creatinine. In summary, the average level of Mn-B was at least twice as high in the Mn-exposed workers than in the controls, while their average urinary excretion of manganese showed a tenfold increase over that of the control group.

Twenty-nine Mn-exposed workers volunteered to give a blood sample before and after the workshift. They were either on morning (n = 17) or on afternoon (n =

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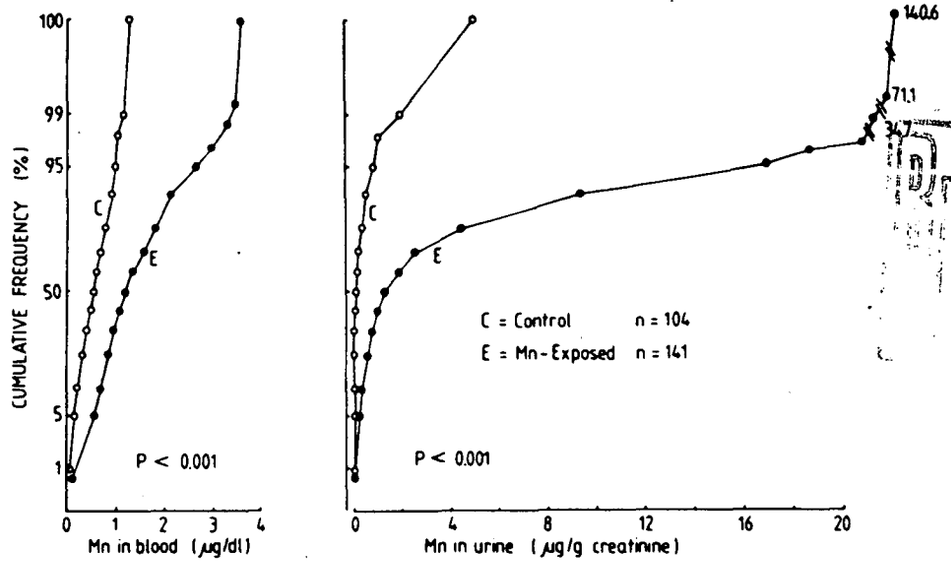

Fig. 2. Cumulative frequency distributions of manganese levels in blood and urine of control and Mn-exposed workers.

12) shift. The Mn-B levels ranged from 0.48 to 3.38 µg/100 ml in the preshift blood samples and from 0.40 to 3.70 µg/100 ml in the postshift blood samples. Paired t test ascertained that there was no statistically significant difference between both sets of samples.

From another group of 13 Mn-exposed workers, spot-urine samples were collected at the end of the work week (on Saturday morning), at which time Mn exposure ceased for 3 days. A second spot-urine sample was collected from the same workers on Tuesday morning just before they resumed work. Figure 3 shows that the urinary excretion of Mn was markedly reduced in all subjects 72 h after cessation of Mn exposure. The geometric mean of the Mn-U levels amounted to 7.2 µg/g creatinine at the end of the work week and dropped to 1.3 µg/g creatinine after 72 h without Mn exposure. The biological half-life of Mn in urine is less than 30 h.

Relationship Between Parameters of External and Internal Exposure to Manganese

On an individual basis. The levels of Mn-B (pre- and postshift) and the levels of Mn-air measured with personal air samplers the same day were available for 24 Mn workers. There was no correlation between these parameters. The levels of Mn-U (during shift) together with current Mn-air levels were available for 34 Mn-exposed workers and again there was no correlation between both parameters. Multiple correlations between Mn-B or Mn-U, on the one hand, and Mn-air and duration of Mn exposure, on the other, did not show any relationship. Furthermore, in the total Mn-exposed group (n = 141), there was no correlation between Mn-U and Mn-B or between duration of exposure to Mn and Mn-U or Mn-B.

On a group basis. The Mn-exposed workers were classified according to three different criteria: a) current Mn-exposure at the workplaces; b) duration of Mn exposure; and c) subjective estimation of past integrated exposure by the chief foreman.

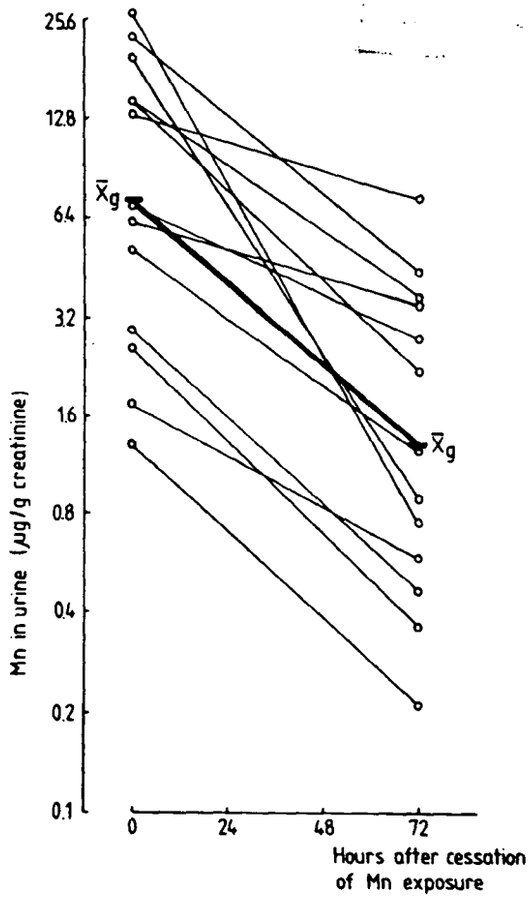

Fig. 3. Levels of urinary manganese determined in a group of 13 Mn-exposed workers at the end of the work week (cessation of Mn exposure) and after 72 h without Mn exposure ($\bar{X}_g$, geometric mean).

Workplaces. Eleven different workplaces were identified in the Mn plant. Table I shows the geometric mean values of the current levels of Mn-air at these workplaces. The mean values of Mn-B (arithmetic) and Mn-U (geometric) of the workers at those workplaces are also indicated. On a group basis there was no correlation between the current Mn pollution at the workplaces and the actual mean levels of Mn in blood, whereas a slight but statistically significant correlation was found with the actual mean levels of Mn in urine ($\overline{\text{Mn-U}}_g = 0.874 + 0.916\ \overline{\text{Mn-air}}_g$; $n = 11$, $r = 0.62$, $P < 0.05$).

Duration of Mn exposure. The group of 141 Mn-exposed workers was divided in four subgroups according to duration of exposure to Mn, ie, < 5, 5–9, 10–14, ⩾ 15 years. The mean values of Mn-B (arithmetic) and Mn-U (geometric) of each subgroup were calculated. No statistically significant relationship was found between the parameters of internal Mn exposure and duration of exposure in the Mn plant.

Subjective estimation of past integrated exposure. Due to frequent job turnover between the 11 workplaces of the Mn plant, it was impossible to calculate each worker's integrated Mn exposure (Mn-air × duration). However, on the basis of the chief foreman's estimation of past Mn exposure of the workers, it was possible

TABLE I. Current Average Levels of Mn in Ambient Air at 11 Workplaces of a Mn Oxide and Salt Producing Plant and the Mean Values of Mn in Blood and in Urine of the Workers Currently Employed at These Workplaces

Workplace	No. of workers	Mn-air[a] (mg/m^3)	Mn in blood[b] ($\mu g/100$ ml)	Mn in urine[a] ($\mu g/g$ creat)
1	18	0.180 (5)[c]	1.02	0.89
2	7	0.345 (4)	1.23	1.15
3	4	0.746 (6)	1.52	2.04
4	10	0.812 (3)	1.40	0.99
5	36	0.979 (21)	1.28	1.51
6	14	0.997 (14)	1.50	3.44
7	9	1.093 (5)	1.69	2.33
8	13	1.209 (6)	1.45	1.29
9	10	1.629 (3)	1.76	1.08
10	14	1.700 (11)	1.22	2.40
11	6	2.586 (2)	1.53	3.74

[a]Geometric mean.
[b]Arithmetic mean.
[c]Number of personal air samplings in parentheses.

to group the workers into six categories graded from 1+ (low exposure) to 6+ (heavily exposed). Among the 141 Mn-exposed workers, 91 had been engaged mainly at jobs belonging to one of the six major groups. There was a significant rank correlation ($r_s = 0.83$, $P < 0.05$) between the subjective estimation of integrated Mn exposure and the levels of Mn-B (arithmetic mean) but not with Mn-U (geometric mean).

DISCUSSION

The present paper deals with the assessment of the external (Mn-air) and internal (Mn-B, Mn-U) exposure to Mn of workers from a Mn oxide and salt producing plant. The relationships between these parameters are examined. The duration of exposure ranged from 1 to 19 years (mean 7.1 years). The average current airborne concentration of Mn (total dust) was about 1 mg/m^3 of air (range 0.07–8.61 mg/m^3). The median Mn-B and Mn-U levels in the Mn workers were approximately two and ten times higher than in the control group, respectively. The Mn concentration in blood did not change during the workshift, whereas the Mn level in urine decreased rapidly after cessation of exposure. The half-life of Mn-U is less than 30 h.

The present results do not reveal any relationship between Mn-B and current Mn concentration in the air, either on an individual or on a group basis. This agrees with the findings of Smyth et al [1973]. Like Horiuchi et al [1970] and Tsalev et al [1977], we did not find any relationship between length of employment and the concentration of Mn in blood. It should be realized that, in view of the different pollution by Mn at various workplaces, duration of exposure is an inappropriate estimate of integrated exposure. However, on a group basis, a statistically significant correlation was found between Mn-B and the subjective estimation of workers' integrated Mn exposure made by the chief foreman. Although efficient homeostatic mechanisms seem to prevent large fluctuations of Mn in blood, the existence of such an association suggests that Mn-B is, to some extent at least, a reflection of the body burden of Mn. Experiments on rats conducted by Keen et al [1983] suggest that whole

blood Mn concentration does not reflect recent exposure but the Mn status of the body tissues. Experiments on monkeys by Ulrich et al [1979] also provide evidence that Mn-B correlates significantly with the level of Mn in kidney and pancreas in the different exposure groups.

Except for the study by Horiuchi et al [1970], most of the other reports on occupational Mn exposure [Rodier, 1955; Penalver, 1955; Jonderko et al, 1971; Smyth et al, 1973] failed to establish relationships between Mn-B (and Mn-U) and the severity of Mn-induced neurological disorders. This was usually attributed to individual susceptibility to the disease and may also partly be due to the use of unreliable methods in the measurement of Mn-B [Valentin and Schiele, 1983]. Our epidemiological results reported in the next paper [Roels et al, 1987] provide some evidence of the existence of dose-response relationships between Mn-B and a few parameters (eye–hand coordination, hand steadiness, Ca in serum). This finding reinforces the suggestion that Mn-B is in some way related to the amount of Mn stored in critical organs.

The levels of Mn-U did not correlate on an individual basis with current levels of Mn in air or duration of exposure. However, on a group basis, the mean levels of Mn-U were related to the current Mn pollution of the workplaces but not to the estimation of past integrated exposure. Other authors have reported an association between increased mean Mn-U levels and levels of Mn in air [Tanaka and Lieben, 1969; Horiuchi et al, 1970; Smyth et al, 1973; Chandra et al, 1981]. In contrast, Järvisalo et al [1983] in a study of five mild steel welders using Mn containing welding rods (Mn-air varied from 0.04–0.14 mg/m^3 to 0.30–2.30 mg/m^3), did not find a statistically significant correlation between the airborne concentration of Mn and Mn-U, at least on an individual basis. However, on a group basis the mean levels of Mn-U (0.75–1.85 μg/l) were significantly higher than those of a control group (0.53 μg/l). It is known that the renal route is of limited importance for the excretion of Mn (probably less than 1%). Furthermore, our data indicate that Mn-U returns rapidly to background level when exposure ceases. Therefore, it is not surprising that neither on an individual basis nor on a group basis was there any relationship between Mn-U and Mn-B.

In summary, the present study indicates that on an individual basis, the determination of Mn-B and Mn-U is of limited value for the biological monitoring of workers exposed to Mn dust. Nevertheless, on a group basis, the risk of excessive accumulation of Mn may be ascertained by measuring Mn-B. Likewise, recent uptake of Mn is likely to lead to a rapid increase in Mn-U, but the quantitative relationship between these parameters cannot yet be established.

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